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NEW HYBRIDS FROM INCOMPATIBLE CROSSES IN DATURA THROUGH CULTURE OF EXCISED EMBRYOS ON MALT MEDIA[1]

By ALBERT F. BLAKESLEE and SOPHIE SATINA

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INCREASINGLY of recent years it is becoming possible to control the activities of the living plant by chemical treatment. The success in doubling chromosomal numbers with colchicine and other stimuli naturally led to an attempt to halve the chromosomal number by some similarly simple treatment. The fact that over two hundred haploids ($1n$) had turned up spontaneously in our cultures of Daturas since 1921 showed that the plant is capable of producing individuals with half the normal $2n$ chromosomal complement. Preliminary attempts to induce the production of $1n$ offspring by treating the unfertilized egg cells with a wide series of stimuli were entirely unsuccessful. In the summer of 1940 the cooperation of Drs. J. van Overbeek and Marie Conklin was secured in a more intensive attack on the problem. Something was learned about the processes involved in embryo development,[2] but none of the stimuli tested induced the production of $1n$ embryos. In the summer of 1941 they attacked the problem from a different standpoint in order to learn more about the factors involved in embryo development and attempted to dig out the young embryos and cultivate them on artificial media. The older embryos could be thus readily cultivated, but the smaller ones (under 0.5 mm in *D.*

[1] Read before the American Philosophical Society, November 19, 1943. Contributions from the Department of Botany, Smith College, New Series, No. 12. This investigation was supported in part by the Carnegie Institution of Washington and by a grant from the American Philosophical Society. The authors are indebted to Margaret Conlin, Jean Cummings, Susanne McLean and Mary Sanders, who as graduate assistants have made a large proportion of the dissections.

[2] J. van Overbeek, M. E. Conklin and A. F. Blakeslee, *Am. Jour. Bot.*, 28: 647–656, 1941.

stramonium) would not grow on the artificial media. Since in some cases the spontaneous (1*n*) haploids which appeared in our cultures had been shown to be twins developed within the same seed envelopes as the normal (2*n*) diploids, it was suggested that in such cases some substance in the normal twin might have stimulated the development of the 1*n* partner and that it might be possible to extract this substance and use it in the artificial media. Dr. van Overbeek suggested rather the use of coconut milk, which is a natural endosperm. With this it was possible to culture stramonium embryos as small as 0.2 and 0.15 mm in diameter.[3] Later with the cooperation of Dr. Haagen-Smit the "embryo factor" in coconut milk was concentrated and freed from a number of contaminating substances which deleteriously affected embryo growth.[4]

In reporting this work[5] it was suggested that such growth of excised embryos on artificial media might ensure the success of many wide crosses hitherto impossible. We now have evidence that this suggestion was well founded and we are utilizing the technique just described in a study of speciation within the genus Datura. To analyze chromosomal changes in evolution of the 10 herbaceous species of this genus, hybrids are necessary in which chromosomes may be matched up and compared. Unfortunately, hybrids between certain species have not heretofore been possible. Some of the blocks to crossability may be mentioned:

(1) Racial differences, presumably due to genes, may prevent hybridization. Thus, the first race of *D. leichhardtii* from Australia crosses readily with *D. discolor* as the pollen parent, but the second race of *D. leichhardtii* from the same country, which is indistinguishable in appearance from the first, gives only arrested embryos when similarly pollinated.

(2) The pollen applied to the stigma of the female parent may fail to germinate. This is not true, however, of pollinations between any of the ten herbaceous species of Datura. Lack of pollen germination does not seem to be an important block to crossability. Pollen of other genera of the Solanaceae, such as Petunia and Nicotiana, for example, have been found to germinate on stigma of *D. stramonium* and to ensure the setting of small but sterile capsules.

(3) The pollen tubes may burst before reaching the ovary and thus the opportunity for fertilization prevented as has been shown by an earlier study of Buchholz[6] *et al.*

(4) The slower growth of pollen tubes of short-flowered species may be a handicap to them in reaching the ovaries of long-flowered Daturas before the styles become withered. Perhaps such crosses could be facilitated by splicing of styles which Buchholz and Doak[7] employed to increase pollen transmission of extra chromosomes in *D. stramonium*.

(5) Fertilization may fail to take place after the pollen tubes reach the ovary. Whether this condition occurs in species crosses in Datura is not known, but not all the incompatible species crosses in the genus have been studied from this standpoint.

(6) Fertilization may occur, but the zygotes abort at an early stage. Thus, in the cross *D. stramonium* × *D. metel*[8] there are abundant fertilizations, but the fertilized egg cell develops to not more than 8 cells before the proembryos become aborted.

(7) Fertilization may take place and embryos develop to a later stage when something arrests their further growth and the imperfect seeds which result are incapable of germination. Of arrested embryos there are two main classes: those represented by the cross *D. inoxia* × *D. discolor* in which a large proportion of the embryos reach a relatively advanced stage before becoming arrested and those represented by the cross *D. inoxia* × *D. stramonium* in which only an occasional embryo in a capsule reaches such an advanced stage.

It is possible to dissect out the hybrid embryos which become arrested after the proembryo stage and to cultivate them on artificial media with the technique developed by van Overbeek and Conklin for normal embryos of *D. stramonium*. The media used contained the necessary salts, vitamins and the "embryo factor" secured from coconut milk. When embryos are small (diameter under 0.5 mm), only slight if any growth occurs without the "embryo factor." We have recently found that powdered malt extract can replace the "embryo factor" from coconut milk if sterilized by filtration instead of by heat.

With the malt media we have gotten growth of hybrid embryos from 11 new species combinations in Datura. By similar embryo culture we have secured species hybrids from combinations which had given only a single viable seed from many hundred pollinations. In addition, the dissection method has enabled us to secure numerous seedlings of certain species the seeds of which without treatment give a germination of only about 0.1 per cent. One aberrant species (*D. ceratocaula*), which is semiaquatic and

[3] J. van Overbeek, M. E. Conklin and A. F. Blakeslee, SCIENCE, 94: 350–351, 1941; *Am. Jour. Bot.*, 29: 472–477, 1942.

[4] J. van Overbeek, *Cold Spring Harbor Symp. Quant. Biol.*, 10: 126–133, 1942.

[5] A. F. Blakeslee, *et al.*, *Carnegie Institution of Washington Year Book*, 40: 214–225, 1941.

[6] J. T. Buchholz, L. F. Williams and A. F. Blakeslee, *Proc. Nat. Acad. Sci.*, 21: 651–656, 1935.

[7] J. T. Buchholz, C. C. Doak and A. F. Blakeslee, *Bull. Torrey Bot. Club*, 59: 109–118, 1932.

[8] Sophia Satina and A. F. Blakeslee, *Bull. Torrey Bot. Club*, 62: 301–312, 1935.

grows in shallow ponds in Mexico, had never hybridized with any Datura. Through use of malt media, however, it has given hybrids with several species among which is *D. stramonium*. In this latter species there have been developed a large series of chromosomal tester races (Prime types) with which the chromosomes in *D. ceratocaula* may be determined. Perhaps our most surprising success of the dissection method is securing hybrids between *D. inoxia* and a tree Datura. This suggests the possibility of extending chromosomal analysis to the group of tree Daturas which by some taxonomists are considered generically distinct from the herbaceous Daturas and to be included in a separate genus, *Brugmansia*.

The excised embryos may be extremely slow in developing in the culture media and for some time after surviving the shock of transplanting into soil, which is often a disastrous experience. Ultimately, however, the hybrids which survive have developed into vigorous plants without sign of weakness.

We have apparently succeeded in getting a new hybrid of Iris (*I. pseudacorus* × *I. versicolor*) from dissection of arrested embryos sent us by Dr. George M. Reed, of the Brooklyn Botanic Garden. We have evidence that the technique described may be of value also in other genera in securing new hybrids which have hitherto been impossible. Moreover, Skirm[9] has recently succeeded in getting a number of new hybrids from the dissection of hybrid embryos of different species of Lilium which appear not to need the aid of the "embryo factor" from coconut milk or malt extract for their development in artificial media.

Systematic study of other genera would be necessary before one would be warranted in taking the genus Datura as typical of the proportion of new hybrids which can be secured in other groups by cultivation of excised embryos. Our experience with Daturas, though incomplete, would suggest alluring possibilities with other forms. With the 10 herbaceous species of Datura there are 90 hybrid combinations theoretically possible if each species is considered separately as male and female parent. The formula is $n(n-1)$. Viable hybrid seed was secured in 18 combinations, a number which might possibly be slightly raised if a large number of pollinations had been made in some of the combinations. In 49 combinations no attempt has yet been made to dissect out arrested embryos or the capsules from recent pollinations have not yet reached a dissectable stage. In 12 combinations dissections have been attempted but without success. In 11 combinations, arrested embryos have been dissected and cultured. Of the 23 combinations actually tested 11, or 48 per cent., have given dissectable embryos which have been brought into cultivation. In attempting to get hybrids from arrested embryos, we have begun with those combinations which would be of most value to our study of chromosomal differences between species, but there is no reason to believe that when the combinations which have failed to yield viable seeds are completely analyzed, the percentage of arrested embryos which can be cultivated will be greatly altered. If we should succeed in our attempts to coax development of the early-aborting embryos, such as those found from the cross *D. stramonium* × *D. metel*, we might be able to secure nearly all the hybrids theoretically possible from the 90 species combinations among our 10 herbaceous Daturas.

The dissection technique may aid in an understanding of the factors involved in chemical regulation of embryo development and new hybrids which it seems capable of supplying may prove useful in genetical analysis of other forms than Datura. They give promise, moreover, of becoming of considerable value economically. Hybrids, especially from wide crosses, are characterized by increased vigor as exampled by the high yields of hybrid corn. Although intermediate forms are common, hybrids may be classified into fertile hybrids and sterile hybrids. The latter are sometimes called "mule plants" since they are like the sturdy mule in that they can not form sex cells since the chromosomes of one parent are too unlike those of the other parents to mate and form pairs; and pairing of chromosomes is necessary for sexual reproduction. Such sterile hybrids may be rendered fertile and pure-breeding with retention of hybrid vigor by doubling chromosome number.[10] In a number of cases sterile hybrids between species have been made fertile through spontaneous doubling of chromosome number which had taken place before recorded history to produce pure-breeding races which had been preserved by prehistoric man because of their superior qualities. Among such fertile "mule plants" may be mentioned our best varieties of wheat, oats, timothy, tobacco and cotton. We no longer have to wait ages for the chance hybridization between species and the later rare spontaneous doubling of their chromosomes in order to secure such superior varieties. With the use of colchicine we can now make them up to order, provided we have the sterile hybrids to start with. The dissection technique should considerably increase the source of these sterile hybrids. These two methods in combination bid fair to be of considerable service in increasing the yield of plant products in a time when need is felt for ways of growing two blades of grass with the labor formerly required to grow one.

[9] G. W. Skirm, *Jour. Hered.*, 33: 211–215, 1942.

[10] A. F. Blakeslee, *Amer. Jour. Bot.*, 26: 163–172, 1939.

In this relatively new field there is opportunity and need for many investigators to explore the range within which artificial cultivation of hybrid embryos is feasible, to improve the technique of such cultivation and to adapt it to the different forms investigated and to study the factors which limit crossability with the aim of still further increasing the possibilities of hybridization.

It should be stated that others have also cultivated hybrid embryos on artificial media. Our contribution to the hybridization problem lies in the use of the "embryo factor" and the application of the technique of van Overbeek and Conklin which enable embryos to be excised and cultivated at an earlier stage, at least in Datura, than has heretofore been possible, and in the use of malt extract as a more convenient source of the "embryo factor" than coconut milk.

Further study of regulatory factors involved in fertilization and embryo differentiation should lead to a conscious control of a wider range of life processes.

USING ELECTRONS FOR MICROANALYSIS

By Dr. V. K. ZWORYKIN

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THE past decade has seen an exceedingly rapid growth of the development and use of electronic tools in all sciences. One of the most spectacular of these is the electron microscope which, with its extremely high resolving power, is able to project man's vision further than was ever before possible towards the direct observation of the building blocks of nature. While our vision has been greatly extended and now enables us to see things in the size range 20 to $10{,}000 \times 10^{-7}$ millimeters, the type of information that we obtain through the sense of vision has not changed in any way; that is, we see the size, shape and structure of the finer details of a specimen but nothing else. Such information is sufficient for the solution of innumerable research problems but it does not represent in any way a complete exploitation of the electron microscope or of the electron optical method. If we are to make full use of what we observe with the electron microscope we must supplement it by the proper application of controlled experiments or by the development of new tools which provide additional information in this same size range.

One of the most specific types of information that would be of immediate use in the field of electron microscopy is that pertaining to the nature or composition of the entities observed. In a large part of the work being carried on with the electron microscope pure samples are used so that the information with regard to shape, size and structure can be tied up immediately with the chemical and physical properties of the material. However, when the electron microscope is applied to problems in which complex or organized structures are present, the different entities observed are spread out in the image and there is no direct way of correlating the composition of a specific particle with a chemical analysis made on the specimen in bulk. A number of methods of attacking this problem have already been suggested and some preliminary work has been done.

One method is the correlation of the intensities of image points with the mass densities of corresponding object points. While the theory of the electron microscope shows that there is a relationship between the mass density of the object and the intensity of the image, it is difficult to obtain an accurate measure of density in this way because of the necessity of knowing accurately the thickness of any given object point. Another discouraging feature of this method is that more often than not intensity anomalies occur in the image as a result of electron interferences which take place if the particles being investigated are crystalline.

Electron diffraction has always been a very useful method of analysis—particularly of powdered chemicals. Unfortunately, like most other methods, it gives an analysis of the whole specimen. Recently, there have been attempts to apply electron diffraction to point analysis. In these methods the irradiating beam is confined to the small areas of the specimen under investigation. While this method shows some promise, it can be applied only in the case of crystalline particles and even in this its usefulness is limited by the fact that the individual particles are almost invariably single crystals. This requires that they have the proper orientation in the specimen before a pattern can be obtained and the pattern produced is that of a single crystal which in itself is not always sufficient for the identification of a compound. The third method which may be applied for identifying the chemical nature of particles is the use of specific reagents which change the mass density of the particles in question. While this method appears to be tedious and not too certain of success in any particular case, some exploratory work in connection with the selective staining of bacteria has been done.

Recently, in a paper to the *Physical Review*, J. Hillier of this laboratory has described a more direct electronic method of attacking the problems outlined above. The paper described a new type of instrument which is named the electron microanalyzer and in

which a fundamentally different method of obtaining a chemical analysis is used.

Throughout the development of the electron microscope it has been realized that the electrons, on passing through the specimen, often lose small amounts of energy due to inelastic collisions with the atomic electrons of the specimen. X-ray theory predicts that if in an inelastic collision one of the electrons from an inner shell of an atom of the specimen is removed, the colliding electron must lose an amount of energy equal to or greater than that found in the subsequently emitted x-ray photon. While this was realized sometime ago, it was only recently that the phenomenon was observed experimentally. Since for each type of atom it takes a discrete and different amount of energy to remove one of the inner electrons, it appears that this phenomena can be used to identify the atoms in a specimen.

The experimental method of doing this is quite straightforward. The specimen is bombarded by a beam of electrons of one velocity and the velocity distribution in the transmitted electrons measured by a suitable means. The position of the peaks on the resulting velocity distribution curve is sufficient to identify the elements present in the specimen. However, in itself, this is not satisfactory for direct application to the problem of identifying individual particles on electron microscope specimens because it gives no information regarding the location of the particles. It is the ability to identify both the elemental composition and the location of an area in a specimen that characterizes the electron microanalyzer.

In the electron microanalyzer electron lenses are used to confine the electron beam to only that area of the specimen which is to be analyzed. Moreover, the area being analyzed and the specimen as a whole can be observed by means of an electron microscope which is incorporated in the instrument. Since both modes of operation of the instrument use the same lens system, the instrument is extremely compact.

As a result of the use of the "probe" method and a high quality electron optical system, it has been possible to greatly enhance the resolving power of the conventional electron velocity analyzer. In fact, in this new instrument, practical limitations on the resolving power are almost completely removed. In the present experimental model the velocity of the transmitted electrons can already be measured to one part in 5,000. Moreover, this resolving power can be increased or decreased at will; the only limitation being in the degree of homogeneity of the incident beam.

At the present time the instrument is being carefully tested using thin films of known materials in order that its possibilities and limitations may be better understood. The velocity distributions which are characteristic of a number of elements have been obtained proving that all the elements up to atomic number 26 can be detected with the present experimental model of the instrument. There seems to be no theoretical reason why this list can not be extended throughout the periodic table.

It is apparent that the major limitation of the instrument at the present time is its inability to differentiate between organic compounds, though there are indications that quantitative measurements on the heights of the peaks in the velocity distribution curve will yield some information in this regard. As in all radically new types of instruments, it is extremely difficult to predict the future uses and applications. It is evident that the microanalyzer is worthy of further investigation. Already the high resolving power which is obtained in this method of velocity analysis points to the possibility of applying it to obtain direct information with regard to collision problems in quantum physics. Added to this is the attractive possibility of obtaining direct elemental analysis of supermicroscopic structures, particularly in biological problems where the location of elements other than carbon, nitrogen and oxygen in the specimen is important.

OBITUARY

WILLIAM EMERSON RITTER: NATURALIST AND PHILOSOPHER[1]

PROFESSOR RITTER had entered his eighty-eighth year at the time of his death a few months ago (January 10). His advanced age must have come as a surprise to many, for as recently as 1938 he had brought out an impressive volume of biological fact and interpretation, and he had contributed to some of our scientific journals even later than that. Ritter got a somewhat delayed start in his scientific career, but he more than compensated for this by exceptional productivity at an age when most of us lapse into silence.

William Emerson Ritter was born in Hampden, Wisconsin, on November 19, 1856. Much of his boyhood was spent on a farm, and to this period of his life he was fond of referring later. It was here, no doubt, that his life-long love of nature commenced. He graduated from the State Normal School at Oshkosh in 1884, and engaged in public school teaching in his native state before carrying his education to higher levels. In 1888 he received his B.S. from the University of California, and his doctorate was attained at

[1] Contributions of the Scripps Institution of Oceanography, New Series No. 223.

Harvard in 1893, when he was 36 years old. In June, 1891, he married Dr. Mary E. Bennett, whom he characterizes in a dedication as "my severest critic and best helper." There is no doubt of the important part which she played in various phases of his career. Ritter's quest of knowledge and adventure took him to Naples and Berlin in 1894–95; later to England, Japan and various points in the Pacific area. He was a member of the carefully selected party of naturalists which comprised the Harriman Alaska Expedition of 1899. His academic positions ranged from that of instructor in biology at the University of California to the headship of the department of zoology, in the same university, a position which he held until he assumed directorship of the Scripps Institution of Biological Research in 1909. He retained a professorship in the department, however, until he was retired as "professor emeritus" in 1923. Ten years later the degree of LL.D. was bestowed both upon Professor Ritter and upon Dr. Mary Bennett Ritter, his wife.

Ritter's first published paper of which I find record dealt with "The parietal eye of some lizards from the western United States,"[2] thus appearing in his thirty-fifth year. Two years later came his doctor's thesis, "On the Eyes, the Integumentary Sense Papillae, and the Integument of the San Diego Blind Fish (*Typhlogobius californiensis Steindachner*)."[3]

Up to nearly 1910, Ritter's biological contributions lay predominantly in the fields of taxonomy and morphology, his special groups being the tunicata and enteropneusta. The texts and figures of these papers (the figures mainly of his own execution, it would seem) bear witness to a high degree of care and thoroughness in his observation and delineation. But questions of interpretation frequently occupied his attention, as is evidenced, for example, by such a title as "*Halocynthia johnsoni* n. sp., a Comprehensive Inquiry as to the Extent of Law and Order that Prevails in a Single Animal Species."[4]

These morphological and taxonomic studies gave place rather early to behavioristic and philosophical ones, and it is probably these last by which Ritter is more largely known. His stature as a biological philosopher can probably be fairly measured only by another philosopher. His writings reveal extensive acquaintance both with the literature of philosophy and of the history of science, such an acquaintance as I believe few living zoologists possess. And they reveal preoccupation with certain philosophical problems throughout much of his life. His association with Howison at the University of California appears to have been partly responsible for this trend, though the viewpoints of the two men differed very widely. Ritter was primarily a naturalist, Howison a subjective idealist.

Ritter's outstanding published work in the field of biological philosophy bears the title "The Unity of the Organism, or the Organismal Conception of Life."[5] This two-volume book has as its "central idea" that "The organism in its totality is as essential to an explanation of its elements as its elements are to an explanation of the organism." The contrary viewpoint he characterizes as the "elementalist" one, and this viewpoint he seems to attribute, in varying measure, to all other living biologists.

The metaphysical implications of Ritter's "central idea" are matters which the present writer is quite unqualified to discuss. That his position is a "vitalistic" one Ritter denies emphatically, and his denial carries conviction. Superficially, at least, there seems to be much in common between his views and ones set forth during several past decades under such names as "emergent evolution," "creative evolution," "creative synthesis" and "holism." He insists upon an all-out physico-chemical basis for vital phenomena, but he equally insists upon the appearance of entirely new attributes only potentially present in the chemical elements.

Ritter challenges the mechanistic physiologist to state just what he means by expressing a vital phenomenon (say a dog's scratching reflex) in "terms" of the physico-chemical elements involved. This "can be done in one and only one way, namely, by adding to the attributes, that is to the 'terms' which inorganic chemistry recognizes in the chemical agents concerned, just those attributes and terms which the dog's scratch reflex requires in order that the elements may explain the reflex." For brevity's sake, he coins the whimsical abbreviation "doscarex" for the reflex in question, and proceeds to discuss the "doscarecious powers of the oxygen, carbon and so forth," so unforeseeable by the mere chemist![6] This is rare humor. Is it not possibly sound philosophy?

In view of these forthright assertions regarding the relations of the organic to the inorganic, it is rather surprising to find Ritter aligning himself with those few biologists who seriously question the ultimate derivation of the former from the latter, and take refuge in such conceptions as the "panspermia" hypothesis of Arrhenius and others. He could scarcely have questioned the force of such contrary arguments as have recently been set forth by Oparin,[7] who removes one of the difficulties in the way of accepting the earlier

[2] *Bull. Mus. Comp. Zool.*, Harvard, January, 1891.
[3] *Ibid.*, April, 1893.
[4] University of California Publications in Zoology, November 15, 1909.
[5] Richard G. Badger, 1919.
[6] "Unity of the Organism," Vol. 2, p. 204.
[7] "The Origin of Life" (Trans. by S. Morgulis), Macmillan, 1938.

chemical origin of living matter by making it plain why this process could hardly be expected to occur under present-day conditions.

"The Unity of the Organism" was surely a valuable contribution to the literature of theoretical biology, and may still be read with profit twenty-five years after its publication. It is packed with important material, interestingly presented, and much of the discussion is still stimulating. Ritter, I think, was disposed to magnify the differences between his own points of view and those held by other biologists whom he characterized as "elementalists," a circumstance which gave to some of his utterances a needlessly disputatious tone. This was accentuated by his failure, at times, to discern the meaning behind the esoteric sounding terminology of the rather bumptious young science of genetics. Again, Ritter's own utterances did not always lack a cabalistic tinge, as when he asserts his belief that "every living individual organism has the value, chemically speaking, of an elementary chemical substance"; and he gives no biochemical grounds for the hypothesis that all manifestations of life, including the psychical ones, "result from the chemical reaction between the organism and the respiratory gases"—oxygen being almost certainly the effective one. Even the format was against the success of "The Unity of the Organism." One does not ordinarily look beneath such small covers for a work of so considerable importance.

Dr. Ritter's last work of book dimensions, and certainly one of his best, was "The California Woodpecker and I," to which we must add the subtitle so characteristic of the author, "A Study in Comparative Zoology, in which are set forth numerous facts and reflections by one of us about both of us."[8] The volume as a whole is as unique as the title, comprising sections designated "Chiefly Woodpeckers," "Chiefly Both of Us," "Mind, Brain, Conduct," and "Chiefly Myself." Here we are taken in review through Ritter's own more than twenty years' observations on the acorn-storing and other instincts of this remarkable bird, followed by excursions into anatomy, physiology, phylogeny, psychology, sociology, epistemology and ethics! The reader may fail to detect any great degree of coherence at all points in the narrative, but that is not necessary to the enjoyment of it.

No account of Professor Ritter's career would be at all complete without considerable mention of the Scripps Institution at La Jolla, which may, to a certain extent, be regarded as his monument. The Scripps Institution for Biological Research was the outcome of a series of endeavors by Dr. Ritter and some others to create a seaside laboratory in connection with the department of zoology at the University of California. These earlier ventures, commencing as far back as 1892, included the establishment of very temporary quarters successively at Pacific Grove, Santa Catalina Island, San Pedro, Coronado and within the village of La Jolla. Building upon the present grounds was commenced in 1909, and two years later the then "San Diego Marine Biological Association" deeded the property to the University of California, under the title "Scripps Institution for Biological Research." Omission of the word "marine" was deliberate.

It was during this period of unrestricted biological outlook that the present writer became a member of the institution's staff, and for many years thereafter my studies of the races of wild mice were regarded as altogether relevant to the liberal, if somewhat nebulous, "program" of the "Biological Station." Indeed, generous funds were allotted to them throughout. Mr. Scripps's own avowed interests were in human problems, and in biological problems only in so far as they might have human implications. At one time he became mildly interested in a project to establish a colony of anthropoid apes upon our campus, and somewhat later even a department of sociology. But neither enterprise got beyond the talking stage. However, Scripps's own support of the institution was primarily in behalf of Ritter. He more than once said that what he and his sister were really doing was "endowing Ritter," but this was probably a bit of Scrippsian hyperbole.

As already intimated, the first plan of Ritter and his associates had in view the building up of a marine biological station. Writing as late as 1911, he stated his program as being, in essentials, "a biological survey of the waters of the Pacific adjacent to the coast of Southern California." Rather a stupendous project those will say who have had anything to do with biological surveys! Later, as stated, the word marine was dropped, and mice and monkeys were regarded as germane to our "program." But the next tack in our institution's somewhat variable course took it well to seaward again. The word "oceanographic" was incorporated into the official name of our station, and the new director, succeeding Dr. Ritter upon his retirement, was selected with particular view to his qualifications in this field.

The motives behind this change on Ritter's part are somewhat inscrutable. Its wisdom, at the present date, is a purely academic question. The Scripps Institution of Oceanography is very much a going concern, even under wartime conditions. Most fortunately the word "oceanography" has been interpreted very broadly by both of Ritter's successors, and biological work, though changed somewhat in scope, has been liberally supported.

Dr. Ritter's cooperation with E. W. Scripps and others in the founding of the well-known scientific news agency, Science Service, can hardly be discussed

[8] University of California Press, 1938.

here, though it is important to note that it was to Ritter to whom Scripps intrusted the task of interesting and organizing the scientific supporters of the enterprise.

To all who really knew him William E. Ritter looms large, not only as a most lovable personality but as a scientist of much originality and forcefulness. His constant interest, both in the scientific achievements and the personal welfare of the members of his staff at the Scripps Institution, was an outstanding feature of our lives throughout his term as director. Every new bit of information gathered by one of us, whatever its subject-matter, seemed to fit in some way into his framework of thought, and often as not served to illustrate some one of his favorite ideas. He was fond of discoursing with us, singly or in groups. These discourses were often stimulating. But we did not always find them easy to follow. Former President Wheeler, of the University of California, once characterized Ritter, so I am told, as "a great soul struggling for utterance." But this epigrammatic description hardly does him justice, for these "struggles" were not infrequently productive of impressive results.

FRANCIS B. SUMNER

DEATHS AND MEMORIALS

GEORGE STEIGER, chief chemist, retired, of the U. S. Geological Survey, died on April 18 at the age of seventy-five years. He joined the survey in 1892 and was chief chemist from 1916 to 1930.

DR. ROGER CLARK WELLS, chief chemist of the U. S. Geological Survey, died on April 19 at the age of sixty-seven years. He had been connected with the survey since 1908, succeeding Mr. Steiger as chief chemist in 1930.

ALBERT HIGGINS SLUSS, professor of mechanical and industrial engineering at the University of Kansas, died on April 17 at the age of sixty-six years.

DR. HERBERT A. CLARK, physicist of the Taylor Instrument Company at Rochester, N. Y., a former professor of physics at Syracuse University, died on April 20. He was sixty-eight years old.

A LIBERTY ship will be named for the late Dr. William E. Ritter, co-founder and honorary president of Science Service. The *S. S. William E. Ritter* will be launched early in May.

SIR ROY FEDDEN will give next month the thirty-second Wilbur Wright Memorial Lecture of the Council of the Royal Aeronautical Society, London.

SCIENTIFIC EVENTS

A GOVERNMENT TESTING LABORATORY IN SOUTH AFRICA

IT is reported in *Industrial Standardization* that in order to safeguard the public and to aid in checking quality and performance of materials and manufactured products, the South African Standards Institution has recommended that a National Standards Testing and Investigational Bureau be set up by the Government. Such a bureau would act as a national standardization laboratory and would carry out or arrange for investigations and tests in connection with standardization. The institution recommended that this bureau be established by Act of Parliament as a corporate body.

The functions of the bureau would include the testing and calibration of precision instruments, gages and scientific apparatus; determining their degree of accuracy with regard to fundamental standards, and issuing certificates with regard thereto. Testing and investigations on behalf of the South African Standards Institution and others would be done either by delegating the work to approved institutions or by providing laboratory facilities. Such testing would include physical or chemical examination of materials and products and tests of their use and performance.

The bureau would also assist the South African Standards Institution in investigating any questions affecting the preparation of its standard specifications. It would provide facilities for testing goods, articles and materials purchased on specification to decide whether such materials comply with the specification, and would act on behalf of the Government in testing locally manufactured and imported goods with a view to determining whether the goods comply with the regulations laid down by the Merchandise Marks Act or any other act and to verify standards. It would also test manufactured products and carry out investigations and inspections to enable the South African Standards Institution and other standardizing bodies to control their marks. In addition to all this, it is suggested that the bureau could also assist the Government departments in any tests which might need to be undertaken.

THE AMERICAN MATHEMATICAL SOCIETY

MEETINGS of the American Mathematical Society are announced for April 28 and 29 at Columbia University, and on the same dates at the Museum of Science and Industry, Chicago. On Saturday, April 29, there will be a meeting at the University of California at Berkeley.

At Columbia University, by invitation of the Pro-

gram Committee, there have been arranged three addresses: on Friday on "Mathematical Aspects of the Boundary Layer Theory," by Professor K. O. Friedrichs, of New York University; on Saturday at 11:00 A.M. on "The Structure of Normed Abelian Rings," by Professor E. R. Lorch, of Columbia University, and at 2:00 P.M. on "Modern Algebra and the Riemann Hypothesis," by Professor André Weil, of Lehigh University. Sessions for research papers have been arranged for Saturday afternoon.

At Chicago, at 2:00 P.M. on Friday, two invitation addresses were planned—one by Professor J. L. Synge on "The Problem of Saint Venant for a Cylinder with Free Sides," and one by Professor I. S. Sokolnikoff on "Torsion and Flexure of Compound Prisms."

At the University of California, on Saturday, there will be addresses by Professor D. H. Hyers, of the University of Southern California and the California Institute of Technology, on "Linear Topological Spaces," and by Professor R. M. Robinson, of the University of California, on "Hadamard's Three Circles Theorem." A symposium on applied mathematics will be held in the afternoon. The program will consist of two addresses: "Hydrodynamical Stability," by Dr. C. C. Lin, and "The Intrinsic Theory of Elastic Plates and Shells," by Dr. Wei-Zang Chien, both of the California Institute of Technology.

THE CHARLES L. MAYER AWARDS

THE National Science Fund of the National Academy of Sciences announces two Charles L. Mayer Awards for contributions on the nature of light submitted before January 1, 1946.

A prize of $2,000 will be awarded for "an outstanding contribution to our basic understanding of the nature of light and other electromagnetic phenomena which provides in terms intelligible to the community of scientists at large a unified understanding of the two aspects of these phenomena which are at present jointly described by wave and by corpuscular theories."

The second prize of $2,000 will be awarded for an outstanding comprehensive contribution to "a logical, consistent theory of the interaction of charged particles with an electromagnetic field including the interaction of particles moving with relative high speeds."

The first award is intended to encourage for the benefit of the non-specialist the interpretation of facts already known to the specialist. It is hoped that the second award will stimulate attack on one of the most fundamental unsolved problems in physics.

In making these awards the National Science Fund will have the assistance of a special advisory committee, consisting of Dr. E. U. Condon, associate director of the Research Laboratories, Westinghouse Electric and Manufacturing Co., East Pittsburgh, Pa.; Dr. Karl K. Darrow, a member of the technical staff of the Bell Telephone Laboratories and secretary of the American Physical Society; Dr. Robert A. Millikan, chairman of the executive council of the California Institute of Technology, and Dr. I. I. Rabi, professor of physics at Columbia University.

Contributions may be submitted to the National Science Fund of the National Academy of Sciences, 2101 Constitution Avenue, Washington 25, D. C.

GRANTS OF THE AMERICAN ACADEMY OF ARTS AND SCIENCES

THE Permanent Science Fund is administered by a committee of the American Academy of Arts and Sciences. At a meeting of the council on April 12, the grants listed below were approved.

To Theodor von Brand and W. Gardner Lynn, Catholic University of America, Washington, D. C., for special equipment for use in the investigation of metabolic rates in turtle embryos, $80.

To Curtis L. Newcombe, associate professor of biology, College of William and Mary, Williamsburg, Va., for assistance in a further study of the larval stages of *Volsellia demissus*, the ribbed mussel, a source of food, $600.

To Frances A. Schofield, adjunct professor of chemistry, Randolph-Macon Women's College, Lynchburg, Va. To provide assistance and expendable materials in a further study of glycogen forming activity of alanine isomers, $500.

To Abraham M. Shanes, instructor in physiology, College of Dentistry of New York University, for assistance in extending a study of bioelectric potentials, $450.

Communications in respect of the fund should be addressed to Professor John W. M. Bunker, Massachusetts Institute of Technology, Cambridge, Massachusetts.

SCIENTIFIC NOTES AND NEWS

DR. ALBERT G. HOGAN, professor of animal husbandry at the University of Missouri and chairman of the department, has been awarded the Mead Johnson and Company Vitamin B Complex Award for 1944 by the American Institute of Nutrition. The award is "in recognition of his pioneer work on certain aspects of the vitamin B complex, work which has progressed successfully for many years and which

has contributed materially to the modern knowledge of vitamin B."

THE Herty Medal of the department of chemistry of the Georgia State College for Women will be presented on May 6 to Dr. James Edward Mills, chief chemist of the Sonoco Products Company, Hartsville, S. C. The medal, named after the late Charles H. Herty, known for his work on the production of paper from southern pine, is awarded annually for an "outstanding scientific contribution to the South."

THE Gold Medal for 1944 of the American Institute of Chemists has been awarded to Dr. Willard H. Dow, president of the Dow Chemical Company, in recognition of his work in making available supplies of magnesium for airplane construction and styrene for synthetic rubber.

DR. ARTHUR STOLL has been awarded the Flückiger Gold Medal in recognition of his scientific achievements in the field of pharmacy. This medal is the highest Swiss award for research work in pharmaceutical science and is bestowed every five years. The Marcel Benoist Prize for 1942 of the Marcel Benoist Foundation for the Furthering of Scientific Research has also been awarded to Dr. Stoll in recognition of his "outstanding contributions to pharmaceutical chemistry, particularly the isolation and synthesis of pure active principles of drugs." This prize is given for a scientific achievement or study which is of importance to human life. It is awarded every five years to a citizen of Switzerland or to an investigator having resided for at least five years in that country. Dr. Stoll has donated the sum of 20,000 francs accompanying the award to a foundation for the furthering of science.

THE Hinchley Medal of the British Association of Chemists has been awarded to Herbert W. Rowell, in recognition of "his long service to the association and his distinguished career in applied chemistry."

DR. E. V. MCCOLLUM, professor of biochemistry at the School of Hygiene and Public Health of the Johns Hopkins University, has been elected a foreign member of the Swedish Academy of Sciences.

DR. WARREN B. MACK, head of the department of horticulture of the Pennsylvania State College, vice-president of the American Society for Horticultural Science, in recognition of work in the graphic arts, has been made an associate of the National Academy of Design.

THE Ohio State University will confer at its spring convocation the doctorate of science on Dr. Thomas Midgley, Jr., of Worthington, Ohio, this year president of the American Chemical Society.

DR. STEPHEN J. ZAND, director of the Vose Memorial Laboratory of the Sperry Gyroscope Company at Great Neck, L. I., has been elected a fellow of the Royal Aeronautical Society, London.

DR. HUGH S. CUMMING, U. S. Surgeon General, retired, director of the sanitary bureau of the Pan American Union, was elected president of the fifth Pan American Conference of National Directors of Health at the Washington meeting, which opened on April 22.

SIDNEY D. KIRKPATRICK, editor of *Chemical and Metallurgical Engineering*, a director of the McGraw-Hill Book Company, has been elected president of the Electrochemical Society.

THE election as president of the Society of Chemical Industry, London, is announced of Dr. Eric Keightley Rideal, F.R.S., since 1930 professor of colloid science at the University of Cambridge. He will take office in July.

THE ninety-first chapter of the Society of the Sigma Xi was established on April 14 at Emory University, with Dr. G. A. Baitsell, national executive secretary, as the installing officer. The ceremonies were attended by some thirty-four official delegates and representatives from other universities. The installation address was given by Dr. E. Carroll Faust, of Tulane University, who spoke on "Some Biological Interrelationships." The following officers were elected: *President,* O. R. Quayle; *Vice-president,* E. L. Jackson; *Treasurer,* Miss E. Papageorge; *Custodian,* W. B. Redmond; *Secretary,* R. T. Lagemann.

DR. CLEMENT C. WILLIAMS, since 1935 president of Lehigh University, will retire on June 30.

DR. HERBERT JOHN FLEURE, professor of geography at the University of Manchester, has been appointed under the Rallman Foundation visiting professor of geography at Bowdoin College for the year 1944–45. He expects to arrive during the latter part of September and will begin his work at the college on October 5 at the beginning of the fall trimester.

DR. JOHN T. TATE, dean of the College of Science, Literature and the Arts of the University of Minnesota, who has been on leave since 1941, has asked to be relieved of administrative responsibilities. On completing his work with the National Defense Research Committee he will return to the university as research professor of physics. He is succeeded as

dean by Dr. T. R. McConnell, professor of educational psychology, who has been acting dean since 1941.

DR. ARNOLD DEMERRITT WELCH, director of the Division of Medical Research of Sharp and Dohme, Philadelphia, has been appointed professor of pharmacology at the Medical School of Western Reserve University.

DR. WILLIAM H. ADOLPH, for the past ten years chairman of the department of chemistry at Yenching University, Peking, has been made acting professor of biochemistry and nutrition in the School of Nutrition of Cornell University.

DR. GEORGE S. AVERY, professor of botany at the Connecticut College, New London, has been appointed, effective in July, director of the Brooklyn Botanic Garden to fill the vacancy caused by the death on August 9, 1943, of Dr. C. Stuart Gager.

DR. LAWRENCE C. CURTIS, geneticist at the Connecticut Agricultural Experiment Station, a member of the staff for fourteen years, will serve as assistant to Stanley L. Morse, agricultural consultant, who is at the head of a food mission to North Africa with the Division of Relief and Rehabilitation of the Foreign Economic Administration. The mission, composed of a group of agricultural experts chosen from various fields, will study the production of food crops in North Africa and the distribution of these crops to the Allies and to liberated countries.

DR. VERN O. KNUDSEN, dean of the Graduate Division of the University of California at Los Angeles, has returned to the university, following a leave of absence of nearly three years to enable him to undertake scientific war work for the Government. He has been active in devising new instruments and techniques of warfare in two of the divisions of the National Defense Research Committee. He will continue his work for the committee in an administrative capacity.

DR. EDGAR DOUGLAS ADRIAN, professor of physiology at the University of Cambridge, gave the second Pilgrim Trust Lecture before the National Academy of Sciences on April 24. He spoke on "Brain Mechanism."

PROFESSOR EDWARD KASNER, of Columbia University, recently gave at St. John's College, Annapolis, lectures entitled "The Golden Section in Mathematics and Art" and "Cartography, Old and New."

THE H. B. Shmookler Memorial Lecture of the Mount Sinai Hospital, Philadelphia, will be given on May 1, at 9 P.M., by Dr. John P. Peters, professor of medicine at Yale University. The lecture will be entitled "Planning for Post-War Medicine."

AT a meeting of the Council of the American Association of Pathologists and Bacteriologists held on April 8, it was voted that, unless unforeseen circumstances arise, the next annual scientific sessions of the association will be held at the University of Chicago on May 4 and 5, 1945. The symposium selected for the meeting is "Infectious Granulomas, exclusive of Tuberculosis and Syphilis." Dr. Wiley D. Forbus, professor of pathology at Duke University, will be the referee.

THE National Science Fund of the National Academy of Sciences announces that the offices of the fund are being moved to the National Academy of Sciences, 2101 Constitution Avenue, Washington 25, D. C., from 515 Madison Avenue, New York City. Headquarters will be established in Washington as of May 1.

THE National Foundation for Infantile Paralysis has made a two-year grant amounting to $34,080 to the School of Health of Stanford University to be used for the support of a school for technicians in physical therapy and for preparing materials for the use of instructors and students. Under this program selected women students will be provided with specialized training.

ACCORDING to the *Journal* of the American Medical Association, on January 12 the Bolivian branch of the International College of Surgeons was founded in La Paz in the presence of the former United States ambassador to Bolivia, Pierre de Boale, and Dr. Ernesto Navarro, vice-president of the University of La Paz. The chairman of this new institution, Dr. Enrique St. Loup, in his inaugural address stated that the Bolivian branch of the institution was founded in response to an invitation received a year ago from the headquarters of the college in Washington, D. C. The program of this first meeting included the exhibition of a La Paz film showing the different phases of a subtotal thyroidectomy.

THE special correspondent of *The New York Times* at Lima, Peru, reports that under an agreement signed by Dr. Constantino Carvallo, Peruvian Minister of Public Health and Social Welfare, and Major General George C. Dunham, assistant coordinator and director of basic economy in the Inter-American Affairs Coordination Office in Washington, D. C., the Inter-American Cooperative Public Health Service will be

continued for three years from July 1, 1944, when the pact signed in 1942 expires. Of the $1,000,000 to be spent on health and sanitation during the period of the new agreement, half is to be provided by Peru and half by the Institute of Inter-American Affairs.

BY the will of Henry E. Sever, the Chicago publisher, St. Louis University will receive the sum of $3,318,000. According to the daily press, Judge Joseph A. Graber, of the Cook County Superior Court, was directed to select a university or college in Missouri and award to it $100,000, plus whatever remained in the estate after other bequests had been made. Four institutions were surveyed by a committee of three members—Kansas City University; Washington University, St. Louis; the University of Missouri, and St. Louis University. It was directed that the bequest be used for the founding of a technological institute to bear the name of the donor. St. Louis University plans to establish the Sever Institute of Geophysical Technology.

AN Institute of Textile Technology has been established in Charlottesville, Va., by trustees representing twenty-eight textile mills in the East. Its purpose is to maintain an educational institution and to promote scientific research and processes related to the textile industry. The charter provides that none of its profits shall go to any member or individual and expressly prohibits its use of propaganda designed to influence legislation. Ward Delaney, of Charlottesville, has been named president. Arthur M. Allen, of Providence, is secretary.

A SCHOOL OF TECHNIQUES will be held this summer at Wellesley College. Its general aim is to enable the men and women who enroll to increase their proficiency in the techniques used in some special field or fields. In science there will be classes in chemistry, biology, geology, physics and mathematics. In addition students will have an opportunity of studying writing and the use of bibliographic material. Courses will be offered in conversation and the translation of foreign languages.

THE first issue has appeared of *Tropical Medicine News,* to be published bi-monthly as the official organ of the American Society of Tropical Medicine under the editorship of Dr. Joseph S. D'Antoni, secretary of the society. The *News* will be issued on about the twentieth of the month in February, April, June, August, October and December, the months in which *The Journal,* also a bi-monthly publication, does not appear.

EFFORTS are being made to produce varieties of potato resistant to disease and suited to conditions in various parts of the British Empire. It has been shown that the diverse qualities desired must be sought among potatoes indigenous to Central and South America, and a large collection of such types, wild and cultivated, has been formed at the School of Agriculture, Cambridge. Lord Nuffield and the trustees of the Nuffield Foundation have now authorized grants of about £9,000 for capital expenditure on this research. The money will be devoted to the housing of the collection and the work connected with it.

Nature writes that "in 1940 the Medical Research Council, the Ministry of Information and the editorial department of the British Medical Association decided to send abroad abstracts of important articles in British medical journals, and Dr. Howard Jones was appointed to do this work under the direction of the editor of *The British Medical Jounral.* By the end of 1941 a British Medical Information Service had been formed, and the British Council, which had supported the work from its inception, took it over as a permanent part of its work. *The British Medical Bulletin* is published in English, Turkish, Portuguese and Spanish, and Dr. Howard Jones, who is now a whole-time officer of the British Council, has made it a valuable addition to medical literature."

IN the course of an address given on March 2 before the London University Conservative Association, Oliver Lyttleton, British Minister of Production, is reported in *The Times,* London, to have said: "In endeavoring to regain its great trading position after the war, to improve the standards of life and to make its contribution towards balanced international trade, we should promote first research and development. The world is not the same world in 1944 as it was in 1939, and it would be different again in 1946. The primary producing countries would become industrialized to some extent. We shall be required to supply a new world with new goods, to fill a new demand with a new product. To do this we must devote our national ingenuity and resources towards research and development. If our scientists and research workers applied to our post-war problems, in a new field of production, the ingenuity they had shown in the war we might well regain the same position that we occupied when we were the first country to apply coal to the generation of power and when we led the world in the development of the railway. The question whether we were to be a poor nation or a rich nation depended entirely upon whether we used our brains or not."

DISCUSSION

SAFETY OF MECHANICAL RESUSCITATION APPARATUS

Preliminary Statement: Immediately following the publication in SCIENCE (December 24, 1943) of an article by the late Professor Yandell Henderson attacking the Council on Physical Therapy of the American Medical Association, a reply was prepared in which it was pointed out that SCIENCE, then edited by J. McKeen Cattell, should have submitted the attack to the council for its reply before publication. Unfortunately, both Professor Henderson and Dr. Cattell became ill and their deaths occurred soon after the publication of the article. This made it necessary for the council to revise its reply.

THE late Professor Yandell Henderson wrote an extensive paper entitled "The Return of the Pulmotor as a 'Resuscitator': A Back-Step toward the Death of Thousands," which was published in SCIENCE for December 24, 1943. He raised the question of the safety, efficacy and dangers of mechanical resuscitators and particularly charged the Council on Physical Therapy with inefficiency, unfair tactics and professional incompetence by accepting the E & J resuscitator.

Some of the statements of Professor Henderson are incorrect, some misleading and others unwarranted. This brief reply is for the information of the medical profession and the public.

Professor Henderson claimed that mechanical devices for artificial respiration known as resuscitators are essentially identical with a device formerly known as the pulmotor. The latter device, he asserted, was discredited by a Committee on Resuscitation from Mine Gases (about 1912), of which he was a member. The council does not propose any defense of the pulmotor, although he, as a member of the council at the time when that body first undertook to investigate resuscitators, was, of course, aware that the modern devices are essentially different from the pulmotor since they incorporate mechanisms for the control of pressure. In the resuscitators accepted by the council, dangerous pressures are not produced and evidence is available to indicate that the maximum positive pressure of 13 mm of mercury created in them is less than that which a human being can voluntarily produce in his own lungs without discomfort.

Professor Henderson wrote, "A delay of even a few seconds while apparatus is being brought and applied may lose a life." With this statement the council is in full accord. The council has urged[1, 3] that attempts should be made to train every competent person in the proper method of administering manual artificial respiration and that such methods should be applied at the earliest possible moment, even when awaiting the arrival of official agencies with such apparatus as they may have available. Manual methods should be applied whether those administering first aid are expecting the arrival of either an inhalator or a resuscitator.

He wrote, "In this respect, the American Medical Association is in direct antagonism to the American Red Cross." Actually the council has never voiced a criticism of any position taken by the American Red Cross regarding artificial respiration; it has repeatedly advocated the Red Cross training of persons giving first aid in the manual methods.

Both the title and the body of the article imply that the use of resuscitating devices will destroy life "by the thousands." The council has made repeated diligent efforts to ascertain instances in which loss of life or injury has been caused by the resuscitators that have been accepted. Not a single instance has been discovered in which either the opinion of a competent clinician or a post-mortem report would support the contention that loss of life or injury occurred due to the use of an accepted resuscitator.

The original reports mentioned by Professor Henderson appeared some thirty years ago and concerned devices the use of which has long since been discontinued. Again and again he was requested to submit a single authentic instance of loss of life because of the use of an accepted resuscitator, but not a single instance was submitted by him.

In his presentation, Professor Henderson insinuated a lack of "moral sense" in members of the Council on Physical Therapy because they accepted resuscitators without examination by any of them and asserts that this has been admitted by members in their letters to him. Actually, in 1937, two members of the council trained in physiology and medicine made careful experimental investigation of this equipment in the laboratories of the universities with which they are associated. Moreover, individual members of the council made independent investigations. Still further, the council consulted extensively with the late Dr. Pol Coryllos,[2] recognized as an authority in surgery of the chest, who had used the E & J resuscitator extensively in his own practice, had published papers concerning its use and had available evidence in the form of motion pictures as records of his experimentation. The records of the Council on Physical Therapy indicate that three other investigators, one of whom is a professor of physiology in one of the leading universities of the United States, submitted information and advice in relationship to the acceptance of the E & J resuscitator. Thirty-nine individual physicians submitted reports of cases which they had treated with this device and the vast majority of such reports were favorable to its use.[3] Dr. Ben Martinez submitted 500

[1] Annual Report: Council on Physical Therapy, *Jour. Am. Med. Asn.*, 118: 1468, April 25, 1942.

[2] P. N. Coryllos, "Mechanical Resuscitation in Advanced Forms of Asphyxia: A Clinical and Experimental Study of the Different Methods of Resuscitation," *Surg., Gynec. and Obst.*, 66: 698, April, 1938.

cases[4] in which newborn infants had been resuscitated with this device. In the consideration of other resuscitating devices additional evidence has been submitted. Finally, reports were made available of incidents in which rescue teams had used the resuscitator, and this material is available as part of the report on the survey of methods for artificial respiration by Dr. Bernard D. Ross.[5]

Professor Henderson referred to the original adverse report which he wrote for the council in May, 1934, on the E & J resuscitator and made the statement, "but at that point unfortunately the E & J Company learned—or were informed—that the report was adverse." The invariable practice of the council is to transmit to any firm which submits equipment a copy of the report on the device whether favorable or unfavorable. In the case of the E & J resuscitator the usual routine was followed.

Again Professor Henderson stated that the original adverse report was suppressed by the Board of Trustees of the American Medical Association. This statement is untrue. In view of further evidence which became available previous to the publication of Professor Henderson's report, the council became convinced that the report should be held in abeyance until further and more extended studies could be made. Again he implied that the ultimate acceptance of the E & J resuscitator was the result of improper influence exerted by the firm on the secretary of the council. This statement is untrue. The decisions of the council are solely those of its members. The secretary of the council does not have a vote for acceptance or rejection. The secretary of the council is not a physician. Such opinions as he submits are purely with relationship to physical or engineering aspects of the devices under consideration.

Again Professor Henderson implied that the secretary of the council did not refer to that body his invitation to delegate a subcommittee to join with him in testing a resuscitator on animals. Here are the facts: A bulletin is sent to all members of the council every two weeks. Professor Henderson wrote on November 30, 1938, that he had borrowed an E & J apparatus and could retain it only until December 15. In the bulletin dated December 8 appeared the reply which was made to him. Actually Professor Henderson acknowledged receipt of this letter on December 13. In the article, Professor Henderson charged that the secretary did not reply. Certainly it was impossible to appoint a subcommittee, arrange a meeting and provide transportation within the fifteen-day limit that he mentioned.

In the booklet of the Council on Physical Therapy called "Apparatus Accepted" appears a statement regarding resuscitators and inhalators and also a complete description of the prone pressure method. Professor Henderson was himself coinventor of the Henderson & Haggard inhalator which he claimed had "never been patented." A patent number appears on the device, but that patent is not assigned to him. The council has accepted the appliance.

The available evidence indicates that by far the great majority of those well informed regarding inhalators, resuscitators or other devices in the field of physical therapy have confidence in the objective attitude and integrity of the Council on Physical Therapy of the American Medical Association.

Members of the Council

J. S. Coulter, M.D., D.T.M., *chairman,* professor of physical therapy, Northwestern University Medical School, Chicago, and chairman of the Subcommittee on Physical Therapy of the National Research Council.

Major Morris A. Bowie, 910 Old Lancaster Road, Bryn Mawr, Pa.

Eben J. Carey, M.D., dean, Marquette University School of Medicine, Milwaukee, Wis.

Anthony C. Cipollaro, M.D., associate in dermatology, New York Post Graduate Medical School, Columbia University, New York.

W. W. Coblentz, Ph.D., D.Sc., radiation physicist, National Bureau of Standards, Washington, D. C.

A. U. Desjardins, M.D., professor of radiology, Mayo Foundation, and head of the Section on Therapeutic Radiology, Mayo Clinic, Rochester, Minn.

Frank D. Dickson, M.D., associate professor of clinical surgery, University of Kansas Medical School, Kansas City, Mo.

W. E. Garrey, Ph.D., M.D., professor of physiology, Vanderbilt University School of Medicine, Nashville, Tenn.

Frank H. Krusen, M.D., professor of physical medicine, Mayo Foundation, and head of the Section on Physical Medicine, Mayo Clinic, Rochester, Minn.

Frank R. Ober, M.D., John B. and Buckminster Brown clinical professor of orthopedic surgery and assistant dean, Harvard Medical School Courses for Graduates, Boston.

George Morris Piersol, B.S., M.D., professor of medicine, Graduate School of Medicine, University of Pennsylvania, Philadelphia.

H. B. Williams, Sc.D., M.D., Dalton professor emeritus of physiology, Columbia University College of Physicians and Surgeons, New York.

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[3] "E & J Resuscitator and Inhalator Acceptable." Report by Council on Physical Therapy, *Jour. Am. Med. Asn.*, 112: 1945, May 13, 1939.

[4] D. Ben Martinez, "The Mechanical Resuscitation of the Newborn: Report of 500 Cases," *Jour. Am. Med. Asn.*, 109: 489–490, August 14, 1937.

[5] Bernard D. Ross, "A Survey of Methods for Artificial Respiration," *Jour. Am. Med. Asn.*, 122: 660, July 3, 1943.

THE OCCURRENCE OF A TETRAPLOID AND TWO TRIPLOID APPLE SEEDLINGS IN PROGENIES OF DIPLOID PARENTS

IT is usually assumed that triploids originate spontaneously with a relatively low frequency in diploid material. The relatively high proportion of triploid apples found among the leading varieties of the world would seem to indicate that certain desirable characteristics in apple varieties may be associated with triploidy itself or that triploids arise spontaneously, presumably through the functioning of unreduced gametes, with a much higher frequency in apples than hitherto has been suspected.

To test the frequency of occurrence of triploids from diploid parents a beginning was made by determining the chromosome numbers of 278 apple seedlings from crosses made during the course of the breeding program at the New York State Agricultural Experiment Station at Geneva. The crosses were made on March 27, 1942, on potted trees in the greenhouse. The seed was stratified and the seedlings started in the greenhouse in the spring of 1943. Just before they were moved into the nursery, in late May, root tips were taken from each seedling for chromosome number determinations. These determinations were made during the winter of 1943–44.

In a population of 146 seedlings from the cross, Delicious × Bedford, 2 triploids were found. In the nursery these made an average growth during the season of 1943. In a population of 94 seedlings from a cross of Macoun × Jonathan, a tetraploid seedling was found. This seedling has disappeared from the nursery either through accident or failure to become established.

If the true frequency of spontaneous occurrence of triploids and tetraploids in apples approaches the frequency here observed in a population of only 278 seedlings, it would seem to be a relatively easy matter to obtain these forms. A larger number of observations are of course necessary before a reliable value for the frequency of occurrence can be established.

JOHN EINSET

NEW YORK STATE AGRICULTURAL EXPERIMENT STATION,
GENEVA

THE CORRECT GENERIC NAME FOR THE SAND FLY

WRITERS of text-books on parasitology and medical entomology have for the past fifty years insisted upon using the wrong generic name for the Psychodid fly which is the vector of Leishmania, *Bartonella bacilliformis* and pappataci fever.

The generic name used in text-books is *Phlebotomus;* whereas, the correct name is *Flebotomus.* Rondani in 1840 (*Mem. Prima Serv. Dipt. Ital.,* p. 12) erected this genus on a species from southern Italy. Why the spelling has changed from *Fle* to *Phle* is not known; unless it was to make it easier to pronounce, as *Phlebotomus* and *Flebotomus* are homonyms.

This mistake should be rectified and the correct name *Flebotomus* should be used. There is no reason to continue with this mistake in our medical and parasitology literature. Careless mistakes of this type are responsible for the over-abundance of synonymy in our taxonomic literature. Furthermore, it is time medical men and entomologists got together and used the same name, *Flebotomus.*

WILLIAM F. RAPP, JR.

CHATHAM, N. J.

THE LONGEVITY OF THE EMINENT

IN a recent article in SCIENCE,[1] Lehman expresses doubt as to the validity of the curvilinear relationship which I had found between mean age at death and the degree of eminence attained by American physicians.[2] He failed, however, to suggest any reason why this should be considered illogical or of doubtful significance. Certainly the medical and biological sciences abound with this type of relationship. There would seem to be no basis for their non-acceptance except for purposes of mathematical correlation.

Lehman also claims that my conclusions were one-sided, with undue emphasis on the late death-age of the most noted physicians and neglect of a similar late age for those receiving least death-column space. It is true that the final paragraph of my article dealt mainly with the advantages to society of a late death-age for its most renowned members, but isn't such emphasis justified?

Lehman has presented no published statistics in this field, but he does state that his unpublished data show no consistent difference in death-age between the great and near-great in various fields of endeavor. However, like Rendich,[3] he failed to divide his material in any one class into more than two groups—the great and the near-great. With only the two observational categories, it is obvious that his data could not bring out even the strongest curvilinear relationships which might be present.

Until some one presents valid evidence to the contrary, acceptance should be given to my findings of late mean death ages for the most eminent and least eminent physicians and a significantly earlier age at death for those of only moderate fame.

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[1] SCIENCE, 98: 270, September 24, 1943.
[2] SCIENCE, 96: 380, 1942.
[3] *Jour. Am. Med. Asn.,* 119: 1041, 1942.

SCIENTIFIC BOOKS

PLANT GEOGRAPHY

An Introduction to Historical Plant Geography. By E. V. WULFF. 1943. Authorized Translation by E. Brissenden. Waltham, Mass.: the Chronica Botanica Co.; New York, N. Y.: G. E. Stechert and Co., pp. xv + 223. $4.75.

IN the great period of DeCandolle, Forbes, Darwin, Hooker, Wallace and Gray, the importance of plant geography was widely recognized; but the developments of ecology in the present century have tended to divert attention from the wider aspects of plant distribution, even although ecology can make important contributions to the problems involved. An introduction to historical plant geography is, therefore, to be welcomed, and should find a place in every general botanical library. It is valuable not only for the data it presents, but because of their bearing on paleobotany, climatic and geological changes, as well as the problems of plant migration, selection, speciation and adaptations for dispersal.

The author is a Russian, who is thus able to introduce to English-speaking readers much Russian work in plant geography as well as an excellent summary of the whole field. It is to be hoped that a *History of the Floras of the World,* which he has also completed, can appear too in an English translation. In the present volume Dr. H. M. Raup has added a compact statement with references to the recent American work, necessitated by the isolations of the war.

The eleven chapters of this book are concerned with such topics as the scope and history of plant geography; areas—their origin, centers and types; the evidence from geographical distribution of hosts and parasites; wind, water and animals as factors in plant dispersal; the migration of species and floras; the historical causes for the present composition of floral areas; and the concept of floral elements.

The author has decided views, which he applies whole-heartedly to the solution of the many complicated problems and puzzles of plant distribution. He accepts the Age and Area conception as one of many factors at work in determining the present distribution of the earth's population of plant species. His discussion of the impact of the ice age on plant distribution in northern latitudes might have been more extended, but this is an introduction to the subject. A feature which he emphasizes is that not only cultivated plants but the weeds which infest them have, through man's partly unconscious action, lost their power of independent existence in competition with wild plants. He holds, with DeCandolle and Willis, that species generally advance very slowly into new areas, the process frequently necessitating a physiological process of acclimatization. This can hardly apply, however, to such species as *Argemone Mexicana,* which can be seen naturalized in India from the Himalayas to Cape Comorin.

In his discusion of methods of dispersal, the author places a minimum value on their efficiency. He points out, for example, that although the gigantic seeds of the double coconut (*Lodoicea*) have for centuries been thrown up on the coasts of the Indian Ocean, yet this palm remains endemic to the Seychelles alone. If ocean currents have not resulted in successful dispersal in this case, can they have done so with the coconut (*Cocos*) or with the seeds of many other plants? It is now generally conceded that man carried the coconut across the Pacific. Even the transport to distant islands of seeds from edible fruits by birds is made to appear very doubtful.

On the other hand, pollen is known to be carried hundreds of miles by winds, reaching over 10,000 feet in the air. Despite this disadvantage, the study of pollen in peat-bogs and other semi-fossilized conditions has acquired great importance in connection especially with post-glacial deposits and the conclusions which can be drawn from them regarding plant distribution. The recent book by Erdtman[1] in the same series is a timely review of the whole field.

Another interesting feature of Wulff's treatment of plant distribution is his acceptance of continental drift as a working hypothesis, made all the more necessary if the plant's "adaptations" for dispersal have such a limited success. Here the last word is likely to be with the geologists, and some of their recent pronouncements indicate that the controversy will be a lively one before it is settled. One geological difficulty appears to be that Pangaea only began to split apart towards the end of the Mesozoic period, although in earlier ages Eurasia (and perhaps also North America) was sundered by the shallow Tethys sea. What produced this belated instability of the previously single continent?

In his foreword, Dr. Merrill points out another difficulty: the genera of plants common to the two hemispheres are but 6.4 per cent. of the total. Whether this is a real difficulty, however, depends largely on the geographical nature of the process of speciation, regarding which, especially in the tropics, we at present know very little.

Wulff admits that Wegener's hypothesis requires modification, and that unsolved difficulties remain regarding the Pacific Ocean. But the facts of distribution clustering around the conceptions of Gondwanaland, Lemuria and Antarctica are so suggestive, and these conceptions solve so many difficulties that the hypothesis is bound to remain very attractive to botanists, especially as it appears to solve also the other-

[1] *An Introduction to Pollen Analysis.* By G. Erdtman.

wise insoluble problem of "shifting of the poles" and accompanying climatic changes.

Apart from all matters of controversy, this volume, with its accumulation of facts and literature, will be of great service to all who are interested in problems of distribution.

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ORGANIC CHEMISTRY OF SULFUR

The Organic Chemistry of Sulfur. Tetracovalent Sulfur Compounds. By CHESTER MERLE SUTER. 858 pp. 6×8½ in. Bound in dark green cloth. New York: John Wiley and Sons, Inc.; London: Chapman and Hall, Ltd. $10.00. 1944.

THE author states in the preface that this book is intended to serve as a reference work for those interested in the chemistry of those organic sulfur compounds which, broadly speaking, may be regarded as derivatives of sulfuric acid. The chapter headings are, therefore: I. Esters of Sulfuric Acid (94 pp.); II. Aliphatic Sulfonic Acids (101 pp.); III. The Preparation of Aromatic Sulfonic Acids (186 pp.); IV. The Properties and Reactions of Aromatic Sulfonic Acids (71 pp.); V. and VI. Derivatives of Aromatic Sulfonic Acids. 1. Sulfonyl Halides, Esters, and Anhydrides (121 pp.), 2. Sulfonamides and Related Compounds (85 pp.); and VII. Sulfones (117 pp.).

Encyclopedic in the field it covers, it is a veritable mine of information. References to all important literature on the subject, as recorded in *Chemical Abstracts* up to January 1, 1942, and totaling many thousands, are included. In recognition of the vast amount of time and labor which the author has expended in the preparation of a volume which makes all organic chemists his debtors, it is to be hoped that the welcome accorded it will be correspondingly cordial and that in due course of time we shall see from his pen other volumes treating with similar thoroughness and skill the remaining branches of the subject.

Each chapter opens with a detailed table of contents, showing the order in which the subject matter is classified and presented, and closes with a consolidated register of the references cited in the text. In addition to these references, there are innumerable tabular lists of compounds distributed throughout the text. Methods of preparation, general properties and reactions, derivatives of various kinds, industrial and medical applications, all are discussed in due course. A comprehensive index (83 pp.) is supplied.

In its chosen domain, the book is *facile princeps*, and is most heartily recommended. In paper, type, printing and binding, the book is fully up to the usual high Wiley standards.

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INDUSTRIAL CHEMISTRY

Industrial Chemistry. By WILLIAM THORNTON READ. 3rd edition. v + 631 pp. New York: John Wiley and Sons, Inc. 1943. $5.00.

THE third edition of Professor Read's well-known volume follows very closely the general plan and arrangement of previous editions.

A first section of six chapters discusses the approach to chemical engineering and serves as an excellent elementary introduction for readers who may be generally interested in the subject or who are approaching it for the first time.

The next four chapters discuss materials and equipment and are designed to give the general reader an introduction to the subjects of unit operations, materials of construction, power plant chemistry and related matter. The remaining seventeen chapters, 450 pages, are devoted to about twenty of the chemical industries of outstanding importance.

The volume represents a thorough revision of the previous editions and brings all the subjects treated up to date except for progress in the war interests. The author notes that the present world situation throws most statistical matter out of balance, and therefore, in general, bases economic data and so forth on the prewar figures.

About thirty pages of new matter have been added, including especially additions in the chapters on rubber, plastics and protective coatings; and, in fact, all the chapters represent much more than a revision of previous manuscript since in most cases the material is entirely rewritten.

The book is very readable, and the concise, entertaining style of the author is evident throughout, though the author has had the cooperation of recognized authorities in each field treated. The book should be welcomed by all those who have found the first and second editions useful and should reach a wide circle of new readers.

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PHYSICAL BIOCHEMISTRY

Physical Biochemistry. By HENRY B. BULL. New York: John Wiley and Sons. iv + 340 pp. $3.75. 1943.

THIS book is a short summary of many physicochemical principles and methods which have been applied in biochemical research. A noteworthy feature is the large number of references to the literature, particularly that of the last decade. More space is devoted to the presentation of principles than to the discussion of their application. While some of the equations are logically derived from fundamentals, many others must be accepted on faith. Particular

mention should be made of the author's discussions of dielectrics, electrokinetics, viscosity, diffusion and membranes, since these topics have been neglected in many elementary text-books.

In general the treatment is clear and accurate, but there are occasional lapses. The definition of the erg (p. 15) is grossly incorrect. The author implies (p. 108) that Harned and Ehlers did not use buffered solutions, while as a matter of fact their precise values for dissociation constants were obtained only by the use of buffer mixtures. A method for extrapolating electromotive force data (p. 110) is presented in a sadly garbled form. The name of the man who formulated the law of diffusion (p. 272) should not be identical with that of an American steel magnate. The method of obtaining partial specific volumes would be more intelligible if the words (p. 292, line 4) agreed with the symbols. However, most of the errors will be caught by a careful reader.

The lectures on which this book was based were probably a pretty stiff dose for the medical and biological students who heard them. The book should be particularly useful to future research workers who are willing to supplement it, as the author suggests, by a generous amount of outside reading.

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SPECIAL ARTICLES

SUPPRESSION OF GROWTH OF THE BROWN-PEARCE TUMOR BY A SPECIFIC ANTIBODY

THE cells of the Brown-Pearce carcinoma possess a distinctive constituent which can be identified *in vitro* through its reaction with an antibody that appears in the blood of certain rabbits implanted with the growth, as previous studies have shown.[1] This constituent is regularly present in large amounts in cell-free, saline extracts of the Brown-Pearce tumor, but it has not been detectable in similar extracts of other rabbit tissues, normal or neoplastic; it is readily sedimentable in the high-speed centrifuge, and certain of its properties suggest that it may be a protein.[1,2] Inquiry has now shown that the antibody which reacts specifically with the distinctive constituent has an influence on living Brown-Pearce tumor cells.

For *in vitro* experiments, serum specimens known from trial complement fixation tests[1] to contain the specific antibody in high titer were procured from "blue-cross" rabbits[4] in which the Brown-Pearce tumor had recently regressed. The sera were mixed with suspensions of living tumor cells, prepared by pressing "healthy" tumor tissue through a 40-mesh monel metal sieve into Locke's solution and allowing the clumps to settle out in a cylinder, the final preparations containing some 20 to 40 individually suspended tumor cells per microscopic field (×400). The mixtures were incubated 2 to 3 hours at 37° C. and then injected into the leg muscles of three or four normal rabbits. Control injections were made at corresponding situations in the same hosts with an equal quantity of incubated mixtures containing tumor cell suspensions and sera from normal rabbits or from rabbits carrying tumors of other kinds (V2 carcinoma;[5] Sarcoma I of Andrewes and Ahlström[6]). The control mixtures gave rise almost always to tumors that reached 2.0 to 3.5 cm in diameter within two to four weeks, whereas the tumor cells incubated with the antibody-containing sera usually failed to grow, though occasionally they formed small nodules.[7]

The effect was specific in that the antibody-containing sera had no influence on V2 carcinoma cells or those of Sarcoma I in concurrent tests. Yet the antisera did not lyse, agglutinate or alter the appearance of the Brown-Pearce tumor cells during 3 hours at 37° C.; and furthermore the proportion of tumor cells stainable with trypan blue (final concentration

[1] J. G. Kidd, *Proc. Soc. Exp. Biol. and Med.*, 38: 292, 1938; *Jour. Exp. Med.*, 71: 335, 351, 1940; *Jour. Bact.*, 39: 349, 1940. See also J. G. Kidd and W. F. Friedewald, *Jour. Exp. Med.*, 76: 543, 557, 1942.

[2] As bearing further on the nature of the distinctive constituent, recent experiments have shown that it is acted upon *in vitro* by purified proteolytic enzymes (chymotrypsin and trypsin), which rapidly render it unable to react with its specific antibody. In addition, Claude and I have found that the distinctive constituent seems to be associated with the "small particles" or cytoplasmic microsomes of the Brown-Pearce carcinoma cells—the finding having a greater interest since the filtrable agent responsible for Chicken Tumor I appears to be associated with the microsomes of fowl sarcoma cells.[3]

[3] A. Claude, *Proc. Soc. Exp. Biol. and Med.*, 39: 398, 1938; SCIENCE, 91: 77, 1940; J. Furth and E. A. Kabat, *Jour. Exp. Med.*, 74: 247, 257, 1941. See also L. Foulds, *Am. Jour. Cancer*, 31: 404, 1937; J. G. Kidd and W. F. Friedewald, *Jour. Exp. Med.*, 76: 543, 557, 1942; A. Claude, *Biological Symposia*, 10: 111, 1943.

[4] English × Lilac—Rockefeller Institute strain, inbred from fertile hybrids.

[5] J. G. Kidd and P. Rous, *Jour. Exp. Med.*, 71: 813, 1940.

[6] C. H. Andrewes and C. G. Ahlström, *Jour. Path. and Bact.*, 47: 87, 1938.

[7] It may be significant that the Brown-Pearce tumor cells do not "protect" the distinctive constituent from the action of the specific antibody, whereas many living cells, notably certain neoplastic ones, provide such protection for viruses.[8]

[8] P. Rous, P. D. McMaster and S. S. Hudack, *Jour. Exp. Med.*, 61: 657, 1935; J. G. Kidd, *Jour. Exp. Med.*, 75: 7, 1942.

1:300)[9] was no greater in incubated mixtures containing specific antisera than in control mixtures with normal sera. The pH of incubated mixtures ranged between 7.95 and 8.08 as determined with the glass electrode, those containing the specific antisera being no more alkaline than the controls.

With a view to testing for an effect of the specific antibody *in vivo*, attempts were made to stimulate its formation in normal rabbits by repeated intraperitoneal injections of watery, cell-free extracts of the tumor. The results were negative when agouti, chinchilla and Dutch hybrid rabbits were employed, though animals of these breeds may manifest the antibody following the growth of Brown-Pearce tumors.[10] In several experiments, however, blue-cross rabbits have developed the specific antibody following three or four intraperitoneal injections with cell-free extracts of the tumor, and all of the animals in which this happened (16 out of a total of 44) proved resistant, generally completely so, to a small "dose" of Brown-Pearce tumor cells implanted intramuscularly 7 to 10 days after the final intraperitoneal injection.[11] By contrast, the blue-cross rabbits that had not developed detectable titers of the antibody as result of the intraperitoneal injections proved quite as susceptible as normal rabbits, the implantations resulting in large growths in most instances. Again the effect was specific in that the rabbits that had developed the antibody and were resistant to the Brown-Pearce tumor cells proved as susceptible as normal controls to implantation with tumor cells of other types (V2 carcinoma, Sarcoma I).

It is common knowledge that the Brown-Pearce carcinoma, like other cancers transplanted in hybrid hosts, is frequently resorbed after having attained considerable size. Yet many animals have overcome it in our experiments without manifesting the specific antibody in detectable titer at any of repeated bleedings, and sera procured from them have failed to influence the later proliferation of Brown-Pearce tumor cells when incubated therewith *in vitro*. Hence it seems plain that regression of the growth, at least as it occurs in many instances, is probably not brought about by the specific antibody.[12] Recent observations have shown, however, that the antibody may influence the course of events when it develops following the implantation of Brown-Pearce tumor cells. For in the rabbits that have developed the antibody in high titer under such circumstances the growths have almost always regressed abruptly within 3 or 4 weeks after the implantations, while, conversely, the animals in which the tumor has grown progressively and metastasized have usually had little or none of the specific antibody in their blood.[15]

The findings as a whole would seem to indicate that the specific antibody is capable of preventing the proliferation of living Brown-Pearce tumor cells,[16] and they are consistent with the view that the distinctive sedimentable constituent with which the antibody reacts may play some part in the proliferative activities of the tumor cells. In further studies to determine whether the cells of other tumors possess distinctive constituents of similar sort, recent observations[21] have indicated that the V2 carcinoma regularly yields a sedimentable substance that is not detectable in extracts of normal rabbit tissues or in those of other

[9] A. M. Pappenheimer, *Jour. Exp. Med.*, 25: 633, 1917; M. N. Richter and E. C. MacDowell, *Jour. Exp. Med.*, 57: 1, 1933.

[10] I. MacKenzie and J. G. Kidd, *Jour. Exp. Med.*, in press.

[11] In this relation, MacDowell, Claude *et al.* observed in two experiments that 5 per cent. and 35 per cent., respectively, of the C58 mice injected intraperitoneally with sedimented materials procured from Line I leukemia cells later survive implantation with tumor cells that overcame the control animals (Carnegie Institution of Washington, Year Book No. 40: 248, 1940–41).

[12] It seems probable that isoantibodies such as those encountered by Gorer and by Lumsden in tumor-resistant mice and rats[13] might be responsible for regression of the Brown-Pearce carcinoma as this usually occurs. However this may be, experiments have shown that the specific Brown-Pearce antibody does not react with extracts of the normal tissues of tumor-bearing, tumor-regressed or normal rabbits, and it does not lyse or agglutinate their erythrocytes—findings which render it unlikely that the Brown-Pearce antibody is an isoantibody of this kind. Nevertheless, it is obvious that genetic or constitutional factors influence the incidence of the specific antibody, though the nature of these factors remains obscure.

[13] P. A. Gorer, *Jour. Path. and Bact.*, 44: 691, 1937; *ibid.*, 47: 231, 1938; *ibid.*, 54: 51, 1942; T. Lumsden, *Am. Jour. Cancer*, 32: 395, 1938. See also reference 14.

[14] M. J. Eisen and W. H. Woglom, *Cancer Research*, 1: 629, 1941.

[15] In an exceptional instance fulminant growth of the tumor brought about death of the host with widespread metastases on the 34th day after implantation, despite the development of a moderately high titer of the antibody between the 18th and 28th days.

[16] The principle is not new in immunology that antibodies may render cells unable to proliferate without altering appreciably their form or other functions, in this respect resembling certain chemotherapeutic agents.[17] Ascoli[18] and Dochez and Avery[19] have studied the "antiblastic" effects of certain antibacterial antibodies, and Taliaferro has described "ablastic" antibodies which prevent reproduction of *Trypanosoma lewisi* in the rat and *T. duttoni* in the mouse, an interesting fact being that the parasites remain alive, motile and capable of infecting new hosts after a sojourn of months in the blood of animals having effective titers of the ablastic antibodies.[20]

[17] H. Dale, *Lancet*, 2: 761, 1941; *Brit. Med. Jour.*, 2: 411, 1943; H. McIlwain, *Nature*, 151: 270, 1943. See also A. J. Clark, in Heffter's Handbuch der experimentellen Pharmakologie, Berlin, Springer, Ergänzungswerk. 4, 1937.

[18] A. Ascoli, *Centr. Bakt. u. Parasit.*, 1, Abt., Orig., 46: 178, 1908.

[19] A. R. Dochez and O. T. Avery, *Jour. Exp. Med.*, 23: 61, 1916.

[20] W. H. Taliaferro, *Jour. Exp. Med.*, 39: 171, 1924; *Am. Jour. Hyg.*, 16: 32, 1932; *Jour. Immunol.*, 35: 303, 1938.

[21] J. G. Kidd and W. F. Friedewald, unpublished experiments.

rabbit neoplasms, including virus papillomas of the type from which the V2 carcinoma originally derived.

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A CONFIRMATION OF THE PRESENCE OF PANCREOZYMIN IN THE DUODENAL MUCOSA*

HARPER and Raper[1] have recently demonstrated that extracts of duodenal mucosa contain two hormonal agencies affecting the external secretory activity of the cat's pancreas. One of these is the familiar secretin; the other, heretofore not characterized, they have termed pancreozymin; their findings indicate secretin to stimulate the production of fluid and bicarbonate by the pancreatic acini, whereas pancreozymin does not affect the output of the inorganic constituents and causes a marked increase in the production of pancreatic amylase. By implication, all the pancreatic enzymes are similarly affected, since a parallelism in their appearance in pancreatic juice or pancreatic extracts has been repeatedly demonstrated. The obvious academic importance and practical implications of these studies by Harper and Raper clearly indicated that a re-examination be made of various fractions obtained in the isolation of secretin as performed in this laboratory,[2] with a view to substantiation of their findings in the dog and extension of their studies to the three chief pancreatic enzymes.

METHODS

Fasted mongrel dogs were anesthetized with sodium pentobarbital, the femoral vein exposed for intravenous injections, and the chief pancreatic duct (Santorini) cannulated. Three of the secretin concentrates previously described[2] served as the stimulating agents employed, including the crude preparation designated SI; the fraction precipitated by aniline treatment of a solution of SI in 80 per cent. acetone, designated AP in the present discussion; and an aqueous solution of the material purified by treatment of SI with aniline, followed by butyl alcohol extraction, which on treatment with picrolonic acid yields a crystalline picrolonate. All materials were free of vasodilator activity; they were injected intravenously, and the first sample following a given injection was discarded, as it served to flush the ducts and cannula of pancreatic juice resulting from a previous stimulation. Enzymes determined included amylase, trypsin and lipase; they were estimated by the methods previously employed.[3] The volume and enzyme responses were noted following injections of pure secretin and of pure secretin plus the AP fraction before and after a six hour incubation with dog serum. The latter procedure was designed to determine whether pancreozymin is inactivated by serum in a manner analogous to secretin.[4]

RESULTS

It was found in every case that purified secretin evoked a secretion poor in enzymes. Either the SI fraction or purified secretin combined with the AP fraction evoked a secretion with a markedly increased enzyme content, all enzymes being similarly affected. Incubation of the AP fraction with serum vitiated its enzyme-stimulating properties. The averaged results are listed in Table 1.

TABLE 1

Stimulus	No. of dogs	Volume	Trypsin		Amylase		Lipase	
			Units per cc	Units total	Units per cc	Units total	Units per cc	Units total
Secretin ..	10	3.0	367	1,101	0.148	0.444	172	516
Secretin + AP	10	3.2	1,403	4,500	0.412	1.320	865	2,760
Secretin + serum treated AP	5	4.1	314	1,285	0.152	0.624	166	680

DISCUSSION

On the basis of the results submitted it is evident that the AP fraction contains a principle which stimulates production of enzymes by the pancreas; and these are washed out in the secretion stimulated by secretin. It is therefore evident that the findings of Harper and Raper are in all respects confirmed by the results of these experiments and that all pancreatic enzymes are equally affected. Thus separation of secretin and pancreozymin was effected by us some years ago, without a recognition on our part that this had been done. The failure of the pancreozymin fraction to stimulate enzyme production after incubation with serum signifies that there is a substance in the blood, probably an enzyme, which with time inactivates pancreozymin.

SUMMARY

Confirmatory evidence has been secured for the existence of pancreozymin, a hormone present in extracts of the duodenal mucosa the effect of which is to stimulate enzyme production by the pancreas. It is separated from secretin by precipitation with aniline, and stimulates equally the formation of the three chief

* Aided by grant from Josiah Macy Jr. Foundation.

[1] A. A. Harper and H. S. Raper, *Jour. Physiol.*, 102: 115, 1943.

[2] H. Greengard and A. C. Ivy, *Am. Jour. Physiol.*, 124: 427, 1938.

[3] M. I. Grossman, H. Greengard and A. C. Ivy, *Am. J. Physiol.*, 138: 676, 1943.

[4] H. Greengard, I. F. Stein, Jr., and A. C. Ivy, *Am. Jour. Physiol.*, 133: 121, 1941.

pancreatic enzymes; it is inactivated by incubation with serum, probably on an enzyme basis.

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CHLORELLIN, AN ANTIBACTERIAL SUBSTANCE FROM CHLORELLA

CULTURES of *Chlorella,* in inorganic nutrient solutions, produce and accumulate a substance that tends to inhibit further multiplication of the cells.[1] Recently extracts containing this growth-inhibiting substance have been prepared in larger quantities than heretofore and have been tested for antibiotic activity against other organisms. These extracts have been found to possess antibacterial properties against both Gram-positive and Gram-negative organisms: *Staphylococcus aureus, Streptococcus pyogenes, Bacillus subtilis, Bacterium coli* and *Pseudomonas pyocyanea* (*Ps. aeruginosa*).

Both *Chlorella vulgaris* and *Chlorella pyrenoidosa,* commonly considered to be different species, were used in these experiments. The cells were cultured in batteries of 5-gallon bottles containing solutions of the conventional mineral nutrients for pure algal cultures. Various proportions and concentrations of these salts were tested. The more dilute solutions, and those containing ammonium nitrogen, were all sterilized before inoculation. With more concentrated solutions,[1] sterilization was not essential when the solutions were continuously illuminated. A mixture of 5 per cent. carbon dioxide in air was bubbled continuously through the cultures. Some cultures were grown under continuous illumination from white fluorescent lamps for about two weeks. Others were grown in a greenhouse under natural illumination for approximately one month, finally being subjected to continuous illumination from fluorescent lamps for two to three days. Best yields of antibacterial substance were obtained from mature cultures which were harvested immediately after the above mentioned period of illumination.

Various methods have been used to obtain extracts containing the active principle. Crude extracts, suitable for determining the biological activity of the inhibitory substance, were prepared by extraction of the cell-freed culture solutions. For these extractions chloroform, 1,2-dichloroethane or benzene have proven superior to other solvents tried. The separated organic solvent, used for extraction, was removed *in vacuo* and the crude extract was obtained as a brown mass, in yields of 1 to 8 mg per liter of cell-free solution. The consistency of the crude extracts varied from a viscous, tacky liquid to a brittle solid. In some instances, extraction of the cell-freed culture solution was preceded by concentration to one half volume by distillation *in vacuo* at bath temperatures of 50–55° C. Thus far adsorption and elution techniques have been inferior to the extraction procedure. Active material has also been obtained from the cell mass. Apparently moderate heat does not greatly affect the yields of the active material.

Biological tests were carried out on clear aqueous extracts of the crude material. To this end the crude material was thoroughly shaken with a small amount of water. Such a procedure has commonly yielded solutions containing 0.03 to 0.1 mg solids per cc. This solution was adjusted to pH 7.0. When tested against *Staphylococcus aureus,* strain 209, in standard cup assay (18 hours at 37° C., diameter of cup 8 mm) 0.2 cc portions of these solutions commonly produced zones of inhibition 18 to 35 mm in diameter. A zone of 45 mm was obtained from extracts of one lot of crude material. Attention should be directed to the fact that only a very small portion of the active principle is extracted in a single treatment by this procedure, for repeated extractions of a given lot of crude material continue to yield solutions showing a relatively high order of antibacterial activity. The same order of activity was observed when strains of *Str. pyogenes* (on blood agar) or of *B. coli* were substituted as the test organism. The strain of *Ps. pyocyanea* that was used is only slightly less sensitive to the action of this antibacterial agent, while the strain of *Bac. subtilis* is more sensitive than the staphylococcus.

Other tests indicate that the active principle may be bactericidal. One tenth of a cubic centimeter portions of 24-hour broth cultures of *Staph. aureus* were added to 5 cc portions of solutions having the same concentration of active principle as were used in the cup tests. Less than 10 minutes contact with the active principle prevented subsequent multiplication of the organisms when transferred to nutrient broth (incubated at 37° C. for 48 hours). Contact of about 20 minutes was required in the case of *B. coli* to achieve the same result. Similar tests in which the bacterial cells were exposed to the solution of the active principle in fresh rabbit serum showed that the bactericidal activity of the active principle is but slightly inhibited in the presence of serum proteins.

The results of numerous experiments carried out over a period of a year and a half show that an antibacterial substance accumulates in uncontaminated cultures of *Chlorella* and that the activity of this substance can be tested by standard bacteriological methods. For convenience of reference it is proposed to designate this substance by the name *chlorellin.* It is recognized that the products thus far obtained repre-

[1] R. Pratt, *Am. Jour. Bot.,* 27: 52 and 431, 1940; 29: 142, 1942.

sent crude extracts. Considerable work will be required to determine fully the range of biological activity and the chemical nature of the active principle. In view of the low and variable yields thus far obtained it is apparent that further work is necessary to determine the optimum conditions for the accumulation and extraction of chlorellin. The cell mass may prove to be a valuable source of the active principle. These investigations are progressing.

Chlorellin is unique in the constantly growing list of antibiotics which have been reported in the literature, because, since it is derived from an autotrophic organism, its production does not entail the use of expensive and troublesome organic culture media, only inorganic salts, carbon dioxide and light being required.

These investigations have been carried out as a cooperative project by staff members of the College of Pharmacy of the University of California and of the Division of Plant Biology of the Carnegie Institution of Washington.

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SCIENTIFIC APPARATUS AND LABORATORY METHODS

NEW INDICATORS TO REPLACE LITMUS IN MILK

THE use of litmus milk has gained wide popularity in bacteriological procedures because of the large number of biochemical reactions that can be determined with one inoculation. It has been our experience to find it very difficult to duplicate the density of the color. This may be due to the fact that litmus is not a single substance but a mixture which varies with the lichen and preparation used.

A search for a single compound which would serve both as a pH indicator and an E_h (oxidation-reduction) indicator in the proper ranges proved disappointing. A combination of indicators was decided upon, and those embodying the most desirable properties both alone and in combination were Chlor Phenol Red (or Brom Phenol Red) for the pH indicator and Methylene Blue for the E_h indicator.

Chlor Phenol Red is a member of the sulfonphthalein dyes which are widely used in bacteriological media. The pH range is from 5.2 to 6.8. Its yellow color on the acid side and red color on the basic side does not mask the reactions of the Methylene Blue. A stock solution is prepared by dissolving 0.1 gram in 10 cc of absolute alcohol.

The Methylene Blue stock solution is prepared by dissolving 0.625 grams (total dye concentration 84 per cent.) in 250 ml of distilled water. The stock solutions are kept in well-stoppered light-tight bottles.

The formula for the preparation of the milk is as follows:

Dry milk powder	90 grams
Chlor Phenol Red (stock solution)	1 ml
Methylene Blue (stock solution)	2 ml
Water	make up to 1 liter

The milk is then sterilized by the fractional method or autoclaved at 15 pounds for 15 minutes. The color of the milk changes to a light pink when strongly heated, but the original color returns as the milk cools.

Autoclaved milk requires a somewhat longer time for acid coagulation, but this is foretold by the very rapid reduction of Methylene Blue in this reaction.

The color changes in the milk as compared with Ridgeway's Color Standards (1912) are summarized as follows:

Uninoculated	Pale Glaucous Green
Slightly acid	Yellowish Glaucous
Acid with reduction	Ivory Yellow
Alkaline	Pale Russian Blue
Alkaline with reduction	Pale Pinkish Cinnamon
Alkaline peptonization	Clear Transparent Red

Inoculation of organisms of known biochemical character readily overcomes confusion in transposing the same reactions found on litmus milk.

This medium has been successfully used in a number of beginning and advanced classes in bacteriology. Students using milk for the first time have no difficulty in determining the reactions which have taken place.

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